REMARKS/ARGUMENTS

Claims 48-54 and 63-75 are currently pending in the above-identified application. Claims 48, 49, 51-53, 63-66, 71, and 72 have been amended as set forth in detail below. Support for these amendments is identified in the following remarks. No new matter is added by these amendments. In view of the amendments and remarks herein, examination and reconsideration of all pending claims is respectfully requested.

Rejections under 35 U.S.C. § 112, second paragraph

Claims 53 and 54 stand rejected under 35 U.S.C. § 112, second paragraph, as allegedly indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The Examiner states that the recitation in claim 53 of the phrase "... having the nucleotide sequence as depicted as SEQ ID NO:7 and having α1→ 2 fucosyltransferase activity..." renders the claim indefinite because "it is well-known in the art that nucleotide sequences *encode* polypeptides that may have enzymatic activity." Applicants respectfully traverse.

Claim 53 recites, in pertinent part, "a cellular fraction of a recombinant cell containing a vector having the nucleotide sequence as depicted as SEQ ID NO: 7 and having α1→ 2 fucosyltransferase activity" (emphasis provided). It is well-known that fractions of cellular material can have various enzymatic activities conferred by the proteins (*e.g.*, glycotransferases) contained therein.

In view of the context of the phrase at issue in claim 53 as well as the knowledge in the art, as set forth above, the skilled artisan reading claim 53 in light the specification would understand the phrase "having α1→ 2 fucosyltransferase activity..." to modify the term "cellular fraction."

While not agreeing with the Examiner's rejection, but in order to further expedite prosecution of the instant application, Applicants have amended claim 53 to recite "...the nucleotide sequence as depicted as SEQ ID NO:7, said cellular fraction containing the recombinant rat α1→ 2fucosyltransferase of (a) [encoded by SEQ ID NO:7] and having α1→ 2 fucosyltransferase activity ...." (bracketed material added for clarification). For the reasons set forth above, Applicants believe that this amendment clarifies that which would be understood by the skilled artisan reading claim 53 in view of the specification. Accordingly, the present amendment is not believed to narrow or change the scope of the claim.

For the sake of consistency among the claims, an amendment corresponding to that set forth above for claim 53 has been made to claim 52, which is not encompassed by the present rejection. Claim 54 is dependent from claim 53 and therefore encompasses all limitations recited therein. Therefore, the rejection of claim 54 is also believed to be mooted.

In view of the remarks and amendment set forth above, Applicants believe claims 53 and 54 to be definite. Therefore, Applicants respectfully request that the Examiner reconsider and withdraw the rejection of claims 53 and 54 as indefinite under 35 U.S.C. § 112, second paragraph.

Rejections under 35 U.S.C. § 102

Claims 48-54 and 63-75 remain rejected under 35 U.S.C. § 102(b) as allegedly anticipated by Holmes *et al.* (*J. Biol. Chem.* 258:3706-3713, 1983).

Applicants note that the present claims recite a method of "preparative synthesis." It is well-known in the art that enzymatic preparative synthetic methods require a large amount of enzyme activity that can typically only be provided by an isolated, highly-enriched enzyme (high specific activity) or a substantial quantity of enzyme produced by recombinant means. As stated in the specification as filed, "enzymatic oligosaccharide synthesis ... has been limited by the difficulty of isolation and enrichment of glycotransferases from natural sources ... [t]hus, there is a need for methods to produce easily isolatable quantities of glycotransferases with high

enzymatic activity." (Specification at page 5, lines 11-14.) As would be understood by the skilled artisan, the crude liver extract disclosed in Holmes *et al.*, while having reasonable purity for analysis of certain enzyme characteristics, would not have had sufficient purity and/or quantity of enzyme to provide the high specific enzymatic activity needed for "preparative synthesis" of the reaction product, as presently recited in the claims. Accordingly, Applicants believe that Holmes *et al.* does not anticipate claims 48-54 and 63-75 under 35 U.S.C. § 102(b).

While Applicants do not agree with the Examiner's rejection, but in order to further expedite prosecution of the instant application, Applicants have amended independent claims 48, 49, 51-53, 63-66, 71, and 72 to recite that the enzymatic reaction is carried out "in the substantial absence of other rat proteins." (Support for this amendment is found in specification at, *e.g.*, Example 6, which describes a $\alpha 1 \rightarrow 2$ fucosyltransferase assay carried out with the recombinant rat enzyme from a transfected, non-rat cell.) The studies in Holmes *et al.* were conducted using a crude homogenate of rat liver hepatoma. Accordingly, Holmes *et al.* does not disclose a method as recited in the present claims as amended.

In view of the remarks and amendments set forth above, Holmes *et al.* does not anticipate claims 48, 49, 51-53, 63-66, 71, and 72. Accordingly, Applicants respectfully request that the Examiner reconsider and withdraw the rejection of claims 48, 49, 51-53, 63-66, 71, and 72 under 35 U.S.C. § 102(b).

Rejections under 35 U.S.C. § 103

Claims 48-54 and 63-75 remain rejected under 35 U.S.C. § 103(a) as allegedly unpatentable over Holmes *et al.* and the common knowledge in the art of protein purification and molecular cloning techniques.

In response to Applicants' previous arguments traversing this rejection, the Examiner has set forth various contentions regarding the teachings of the cited art, Applicants' reliance on relevant case law, and the basis for the instant rejection. First, the Examiner believes that a "general suggestion in the art" for "making a recombinant enzyme" (emphasis added) to be

a sufficient teaching or suggestion in the art of a recombinant α1→ 2 fucosyltransferase having the particular amino acid sequence as specified in the claims. Second, the Examiner believes that Applicants have "over-applied" the decisions of *In re Deuel* and *In re Bell* because the claims are directed to a polypeptide. Finally, the Examiner believes that the present rejection does not rely on principles of inherency and that Applicants' remarks regarding inherency and obviousness are thereby allegedly rendered moot. Each of these contentions is addressed in detail below.

First, with regard to whether the Examiner has relied on principles of inherency in the rejection under 35 U.S.C. § 103, Applicants note that each of the present claims recite a specific amino acid sequence for the recombinant α1→ 2 fucosyltransferase, or a nucleotide sequence encoding the amino acid sequence. The Examiner does not dispute the fact that the recited amino acid and polynucleotide sequences were not known as of the effective filing date of the instant application. Yet the Examiner attempts to reconstruct the present claims from art which does not disclose the recited sequences. Thus, the Examiner attempts to predicate an obviousness rejection under 35 U.S.C. § 103 on that which was not known or explicitly disclosed as of the effective filing date. For these reasons, irrespective of the technical form of the Examiner's argument, the Examiner's rejection appears to rely on inherency, and Applicants' previous arguments regarding the impropriety of reliance on inherency in an obviousness rejection are relevant to the instant case.

Second, because a determination of whether a claim is obvious under 35 U.S.C. § 103 requires that *all* limitations of the claims be considered and given weight, MPEP § 2143.03, a teaching or suggestion of the recited recombinant enzyme, having the specified amino acid sequence, requires a teaching or suggestion of the amino acid sequence itself. A "general suggestion" for "obtaining" a recombinant form of an enzyme is not sufficient. "Obviousness *cannot be predicated on what is not known* at the time the invention was made." MPEP § 2141.02 (citing *In re Rijckaert*, 28 USPQ2d 1955 (Fed. Cir. 1993)). As noted above, the claims explicitly recite a recombinant α1→ 2 fucosyltransferase having a specific amino acid sequence,

and none of the cited art teaches or suggests the particular recited amino acid sequences of a rat α1→ 2 fucosyltransferase.

Applicants maintain that the court decisions set forth in *In re Deuel* (34 USPQ2d 1210 (Fed. Cir. 1995)) and *In re Bell* (26 USPQ2d 1529 (Fed. Cir. 1993)) are applicable to the instant case. The Examiner contends that these cases are not relevant here because the present claims recite a method of using a polypeptide and not do claim a polynucleotide. It is respectfully submitted that this line of argument can only hold if preparative synthesis of a protein product from the recombinant polynucleotide did not require knowledge of a polynucleotide encoding the protein, which it does.

Applicants respectfully note that the Examiner has not refuted the following, as set forth in Applicants' previous response:

(1) "the existence of a general method of isolating cDNA or DNA molecules is essentially irrelevant to the question [of] whether the specific molecules themselves would have been obvious," *In re Deuel*, 34 USPQ2d at 1215 (reaffirming *In re Bell*, 26 USPQ2d 1529);

(2) achieving a recombinant polypeptide requires knowledge of a polynucleotide encoding it; and

(3) a specific product that requires a specific, unobvious starting material is not rendered obvious by knowledge of a general process for obtaining the product, *see, e.g., In re Ochiai*, 37 USPQ2d 1127, 1131 (Fed. Cir. 1995).

Despite the undisputed principles set forth above, the Examiner continues to take the position that the claims, reciting a preparative synthesis method using a particular recombinant α1→ 2 fucosyltransferase, are obvious even though polynucleotides encoding the particular enzyme were not known or obvious at the time of the invention. It appears that the basis provided by the Examiner for this position is that the claims themselves, although reciting

the particular amino acid sequence for the recombinant enzyme, do not actually recite a method of using the polynucleotides encoding the enzyme.

Applicants respectfully submit that whether the claims recite a method of using a recombinant polypeptide or a polynucleotide encoding it does not change the fundamental relationship between the polypeptide and the polynucleotide, nor the well-established principles set forth above. The pending claims recite preparative synthesis methods comprising use of a recombinant rat enzyme substantially without other rat proteins. The preparative synthetic method is only possible if a sufficient quantity and/or quality of the enzyme is available, such as by use of a recombinant method for producing a recombinant form of the enzyme, and the recombinant form of the enzyme is only possible with specific knowledge of the amino acid sequence of the rat enzyme or a polynucleotide encoding it. Therefore, a teaching or suggestion in the art of the recombinant enzyme as recited in the claims requires, at the very least, a specific teaching in the art of the amino acid sequence or a polynucleotide encoding it. To contend otherwise by alleging that the recited recombinant $\alpha 1 \rightarrow 2$ fucosyltransferase is obvious, even though achieving it requires the presence in the art of a material which was not known or obvious, is inconsistent with and, indeed, contravenes the principles set forth by the Federal Circuit in *In re Deuel* and *In re Bell.*

For the reasons set forth above, as well as for reasons previously set forth in Applicants' previous response filed March 29, 2004, Applicants believe that the present claims are non-obvious over Holmes *et al.* and the common knowledge in the art of protein purification and molecular cloning techniques. Therefore, Applicants respectfully request that the Examiner reconsider and withdraw the rejection of claims 48-54 and 63-75 under 35 U.S.C. § 103(a).

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance and an action to that end is respectfully requested. If

the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 206-467-9600.

Respectfully submitted,

Dated: 20 December 2004 By: Brian W. Poor

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